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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 100911-1 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/SE2004/000350	International filing date *(day/month/year)* 10.03.2004	Priority date *(day/month/year)* 14.03.2003
International Patent Classification (IPC) or both national classification and IPC C07D243/24		
Applicant ASTRAZENECA AB et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.09.2004	08.06.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kollmannsberger, M Telephone No. +49 89 2399-7364

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/SE2004/000350

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-92 as originally filed

Claims, Numbers

1-53 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-10,12-21, 23-32; 39-46; 48,50,52

   because:

   ☒ the said international application, or the said claims Nos. 39-46 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 48,50,42 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-10,12-21, 23-32

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	11,22,33,34-47.49,51,53
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	11,22,33,34-47.49,51,53
Industrial applicability (IA)	Yes:	Claims	11,22,33,34-38,47.49,51,53
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III-1. No search has been carried out for the subject-matter of claims 1-10, 12-21 and 23-32 (see box I of the WO-ISA, form PCT/ISA/237). No opinion can thus be given on these claims (cf. Rule 66.1(e) PCT).

III-2. Claims 39-46 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

III-3. Claims 48, 50 and 52 fail to define the products/starting materials of the claimed processes. These claims are thus so unclear (Art. 6 PCT) that no meaningful opinion can be given.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V-1. State of the Art

The following documents are considered relevant:

D1: WO 98 28268 A2
D2: WO 99 67221 A1
D3: WO 00 07995 A1
D4: WO 01 72324 A1
D5: WO 01 68655 A2
D6: WO 97 24339 A1

V-2. Novelty (Art. 33(2) PCT):

The example compounds of claims 11, 22 and 33 are not specifically disclosed in the cited documents. These claims are thus novel. The same holds for the process claims 49, 51 and 53 since they relate to the preparation of such specific compounds.

Claims 34-47 are also considered novel over the cited documents for the following reasons:

D1 and D2 disclose compounds for medical uses (in particular compounds which inhibit amyloid-beta production) which generically encompass the present claims (see claims of D1 and D2). However, there is no specific disclosure of compounds which have an aryl/heteroaryl substituent attached to a non-condensed caprolactam ring (or the dehyrrated derivatives) as required by the provisos for R2-R6 in the present claims. Claims 37-47 can thus be seen as a novel selection from the disclosure of D1 and D2.

D4-D6 also do not disclose compounds having an aryl/heteroaryl substituent attached to a non-condensed caprolactam ring.

The compounds of D3 differ essentially in the amino side chain attached to the caprolactam ring.

V-3. Inventive step (Art. 33(3) PCT)

Closest prior art is seen in D1/D2 since the compounds disclosed therein present the same use and encompass the present claims generically.

The problem to be solved in view of D1 and D2 is the provision of further compounds useful for the inhibition of amyloid-beta production. The present claims are considered an obvious solution to this problems since they represent a mere selection of compounds already disclosed as being useful for this purpose in D1 and D2. It is noted that aryl substituents at (condensed) caprolactam rings are known to be suitable from e. g. D1 (see table 5-1) and also the equivalence of condensed and non-condensed caprolactams has been shown in these documents.

In the absence of any unexpected effect assiciated with the present selection of

compounds claims 11, 22, 33, 34-47 are not considered to fulfil Art. 33(3) PCT.

The same holds for claims 49, 51 and 53 since the preparation processes are only considered to be inventive if they relate to novel and inventive end products.